CHEST

Sepsis-Induced Cardiomyopathy

Mechanism, Prevalence, Assessment, Prognosis, and Management

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TOPIC IMPORTANCE: Sepsis-induced cardiomyopathy (SICM) is a heterogeneous cardiovascular dysfunction associated with sepsis and septic shock. Although traditionally defined by reversible left ventricular (LV) systolic dysfunction, recent evidence has revealed a broader spectrum, including LV diastolic dysfunction, hyperdynamic LV systolic states, and right ventricular (RV) injury, occurring independently or in combination. Despite their prognostic significance, these phenotypes remain underrecognized and understudied.

REVIEW FINDINGS: The pathophysiology of SICM involves inflammatory cytokines, mitochondrial dysfunction, altered coronary microcirculation, and dynamic changes in loading conditions. Echocardiography, because it is widely available, noninvasive, and capable of comprehensive hemodynamic evaluation, has become the primary modality for assessing cardiac function in sepsis. Emerging measures, including longitudinal LV function and ventriculo-arterial coupling, supplement the LV ejection fraction or other conventional parameters. The inherent differences in sensitivity and specificity in diagnosing myocardial dysfunction along with inconsistent definitions have led to wide variability in reported prevalence. New-onset LV systolic dysfunction occurs in approximately 5% to 32% of patients with sepsis, whereas LV diastolic dysfunction and RV injury are reported in 20% to 57% and 18% to 79%, respectively. All these cardiac phenotypes are associated with significantly increased mortality. Management requires phenotype-guided, individualized approaches rather than standardized resuscitation strategies.

SUMMARY: SICM comprises a spectrum of cardiac abnormalities, including LV systolic dysfunction, hyperdynamic LV function, diastolic dysfunction, and RV injury. Although no targeted therapies have shown survival benefit, recognition of SICM phenotypes is crucial. A tailored, phenotype-guided approach may optimize management.

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KEY WORDS: sepsis; sepsis-induced cardiomyopathy; sepsis-induced myocardial dysfunction; septic cardiomyopathy; septic shock

ABBREVIATIONS: BNP = B-type natriuretic peptide; e′ = early diastolic mitral annular velocity; E/e′ ratio = ratio of early diastolic mitral inflow velocity to early diastolic mitral annulus velocity; GLS = global longitudinal strain; LV = left ventricular; LVEF = left ventricular ejection fraction; LVOT-VTI = left ventricular outflow tract velocity time-integral; MAPSE = mitral annular plane systolic excursion; MCS = mechanical circulatory support; PA = pulmonary artery; PAOP = pulmonary arterial occlusion pressure; PEEP = positive end-expiratory pressure; NT-proBNP = N-terminal pro-B-type natriuretic peptide; RV = right ventricular; RV-FWS = right ventricular free wall strain; RVEDA/LVEDA = ratio of right ventricular end-diastolic area to left ventricular end-diastolic area; SICM = sepsis-induced cardiomyopathy; TDI = tissue Doppler imaging; V-A = ventriculo-arterial

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Sepsis-induced cardiomyopathy (SICM) was first described by Parker et al[1] > 4 decades ago as an acute, reversible myocardial depression. However, it remains underrecognized and poorly characterized due to inconsistent diagnostic criteria and heterogeneous clinical presentations. However, recent advancements in critical care echocardiography have reshaped our understanding, revealing that SICM is not just associated with a depressed left ventricular (LV) function as was classically described. SICM encompasses a broader spectrum, including LV and/or right ventricular (RV) involvement with systolic and/or diastolic dysfunction, which may occur independently or concurrently. Emerging evidence also suggests that hyperdynamic systolic function, traditionally viewed as a compensatory or benign response, might constitute a pathologic variant of SICM with significant prognostic implications.[2]

Despite increasing recognition of this complexity, studies adequately characterizing how myocardial dysfunction evolves through sepsis and providing insights into optimal assessment and management remain scarce. The aim of this review therefore was to synthesize current evidence on mechanisms, assessment tools, prevalence, prognosis, and therapeutic strategies, offering a comprehensive framework for clinicians and researchers.

Literature Search

A search was conducted on MEDLINE using the following search words for the pertinent articles: "septic cardiomyopathy" (1,182 results), "sepsis-induced cardiomyopathy" (526 results), and "sepsis-induced myocardial dysfunction" (690 results). The search was updated on June 23, 2025.

Evidence Review

Mechanisms

The pathogenesis of SICM involves multiple biochemical pathways, including pathogen-associated molecular patterns, inflammatory cytokines, nitric oxide, and damage-associated molecular patterns (e-Table 1). Mitochondrial dysfunction due to structural damage, oxidative and nitrosative stress, proton leak (mitochondrial uncoupling), alteration in mitochondrial permeability, abnormal mitochondrial calcium homeostasis, and incomplete autophagy has also been described as a potential mechanism of SICM[3] (e-Table 2). Although not always apparent at the bedside, these mechanisms offer insight into the biology of myocardial dysfunction in sepsis (Fig 1).

In patients with sepsis, coronary blood flow often remains preserved or even increased. Studies have shown maintained myocardial lactate extraction but a decreased coronary arteriovenous oxygen content difference, suggesting microvascular functional shunting,[4] a protective mechanism similar to myocardial hibernation, that conserves energy during metabolic stress. Impaired oxygen extraction may also result from mitochondrial dysfunction,[3] contributing to the development of cardiomyopathy.

Although not a direct mechanism of SICM, acute changes in cardiac loading conditions can significantly affect the initial clinical presentation and recognition of SICM. For example, fluid resuscitation modifies preload and cardiac filling,[5] whereas vasopressors increase afterload. In the presence of impaired relaxation, fluid resuscitation may contribute to pulmonary edema and reduced LV compliance. A previous study has shown an inverse relationship between afterload and LV systolic function.[6] Sepsis-induced vasoplegia typically decreases afterload, potentially leading to overestimation of LV systolic function and obscuring SICM diagnosis, which may become apparent once afterload is increased with vasopressors. In contrast, increased afterload from vasopressors may result in ventriculo-arterial (V-A) decoupling, in which impaired LV contractility fails to match systemic vascular resistance,[7] ultimately reducing cardiac output. In severe cases, profound vasoconstriction and microvascular dysfunction can lead to digital or limb ischemia, which can further influence perfusion distribution. These dynamic hemodynamic shifts, although not causative, complicate the bedside identification of SICM and must be accounted for when interpreting cardiac function in patients with sepsis.

RV injury can occur with or without concomitant LV dysfunction.[8] RV injury may represent a direct manifestation of SICM,[9] but distinguishing this from RV injury driven by mechanical ventilation-related hemodynamic changes is often challenging. Positive

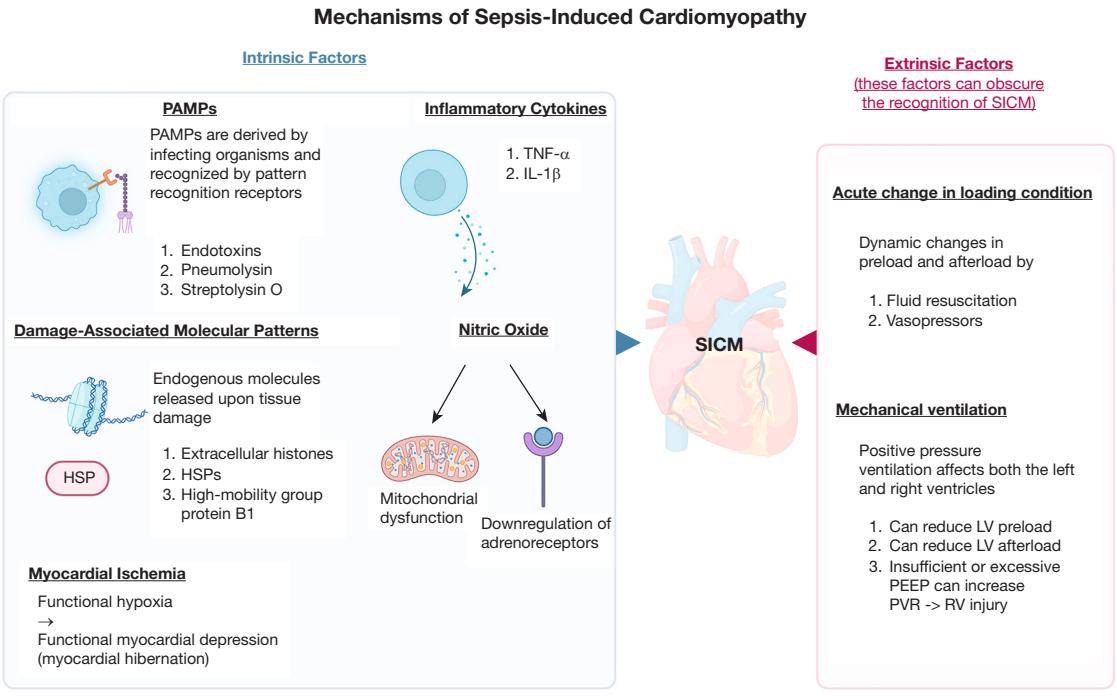

Figure 1 – *Proposed mechanisms of sepsis-induced cardiomyopathy. HSP = heat shock protein; LV = left ventricular; PAMP = pathogen-associated molecular pattern; PEEP = positive end-expiratory pressure; PVR = pulmonary vascular resistance; RV = right ventricular; SICM = sepsis-induced cardiomyopathy; TNF-α = tumor necrosis factor-α. Created with BioRender.com (Sato R; 2025; https://BioRender.com/r88k923).*

pressure ventilation decreases LV preload by limiting venous return and decreases LV afterload by increasing intrathoracic pressure. In contrast, elevated positive end-expiratory pressure (PEEP) can increase RV afterload by compressing alveolar vessels, whereas insufficient PEEP may result in alveolar collapse and hypoxic vasoconstriction, which can also increase RV afterload. Thus, both overdistention and alveolar collapse can contribute to RV injury. Although higher PEEP may be necessary in patients with poor lung compliance, PEEP de-escalation has been associated with improvements in RV function, particularly when respiratory compliance is preserved.[10] Lower respiratory compliance, higher driving pressure, larger tidal volume, and higher plateau pressure have all been associated with an increased risk of acute cor pulmonale and RV injury.[11-13] Furthermore, hypoxia and hypercapnia induce pulmonary arterial vasoconstriction, further increasing RV afterload. Collectively, these mechanical ventilation and gas exchange effects may obscure the clinical recognition of RV involvement in SICM.

Prevalence

A lack of a standardized definition and inconsistent diagnostic modalities have contributed to substantial variability in recognizing and diagnosing SICM, thereby hindering accurate prevalence estimates. The reported prevalence of SICM is also influenced by factors such as premorbid cardiac function, the severity of the septic process, timing of assessment, loading conditions, and the echocardiographic methods used to assess myocardial function. Conventional SICM, defined as new-onset LV systolic dysfunction occurring within 72 hours of sepsis onset, has reported prevalence ranging from 5% to 32% with a pooled prevalence of approximately 20% among patients with sepsis.[14] Hyperdynamic LV systolic function has been observed with a similar pooled prevalence of about 18%, although far fewer studies have specifically addressed this phenotype.[2]

LV diastolic dysfunction appears even more common, reported in approximately 48% of patients with sepsis.[15] A recent large prospective study confirmed a high prevalence of LV diastolic dysfunction, observed in 76% of patients between day 1 and day 3 of sepsis.[16] Notably, current guidelines presume a systematic association between LV systolic and diastolic dysfunction,[17] and such assumptions may be contributing to the high prevalence of sepsis-induced LV diastolic dysfunction. RV injury, encompassing both RV systolic dysfunction and RV dilatation, has been reported in approximately 35% of patients with sepsis.[18]

However, as with LV dysfunction, reported prevalence rates for both LV diastolic dysfunction and RV injury vary widely in meta-analyses, ranging from 20% to 57% and 18% to 79%, respectively,[15,18] reflecting the same limitations in diagnostic consistency.

Assessment of Myocardial Function in SICM

Echocardiography, because it is widely available, noninvasive, and capable of comprehensive hemodynamic evaluation, has become the primary modality for assessing cardiac function in sepsis. This section discusses relevant echocardiographic parameters (Fig 2), cardiac MRI, and biomarkers.

Echocardiography: LV Systolic Function: LV ejection fraction (LVEF) is the most common parameter assessing LV systolic function. SICM has traditionally been defined as a new-onset reduction in LVEF ($< 50\%$) or a $> 10\%$ decrease from baseline during sepsis,[19] with hyperdynamic LV systolic function defined as LVEF $\geq 70\%$.[2] Despite its common use, LVEF is limited by its dependency on preload and afterload, which can vary substantially during sepsis.[20] Clinically, LVEF does not directly reflect stroke volume or cardiac outputs. LV outflow tract velocity time-integral (LVOT-VTI) is a surrogate for cardiac output or stroke volume; a low LVOT-VTI combined with reduced LVEF suggests reduced cardiac output or stroke volume as a result of myocardial dysfunction in preload-optimized patients.

Longitudinal systolic function assessment may have higher sensitivity for detecting subclinical dysfunction than LVEF.[21] The mitral annular plane systolic excursion (MAPSE), measured using a simple M-mode,[22] and the tissue Doppler imaging (TDI)-derived mitral s' wave velocity (TDI mitral s') correlate closely with LV longitudinal systolic function. TDI mitral s' (> 11 cm/sec[23] or > 9 cm/sec[24]) has also been used to define hyperdynamic LV function and might be considered when LVEF is not feasible. These parameters are particularly useful in patients who are mechanically ventilated, in whom limited endocardial visualization often hampers accurate LVEF measurements with Simpson's method. Although MAPSE and TDI mitral s'

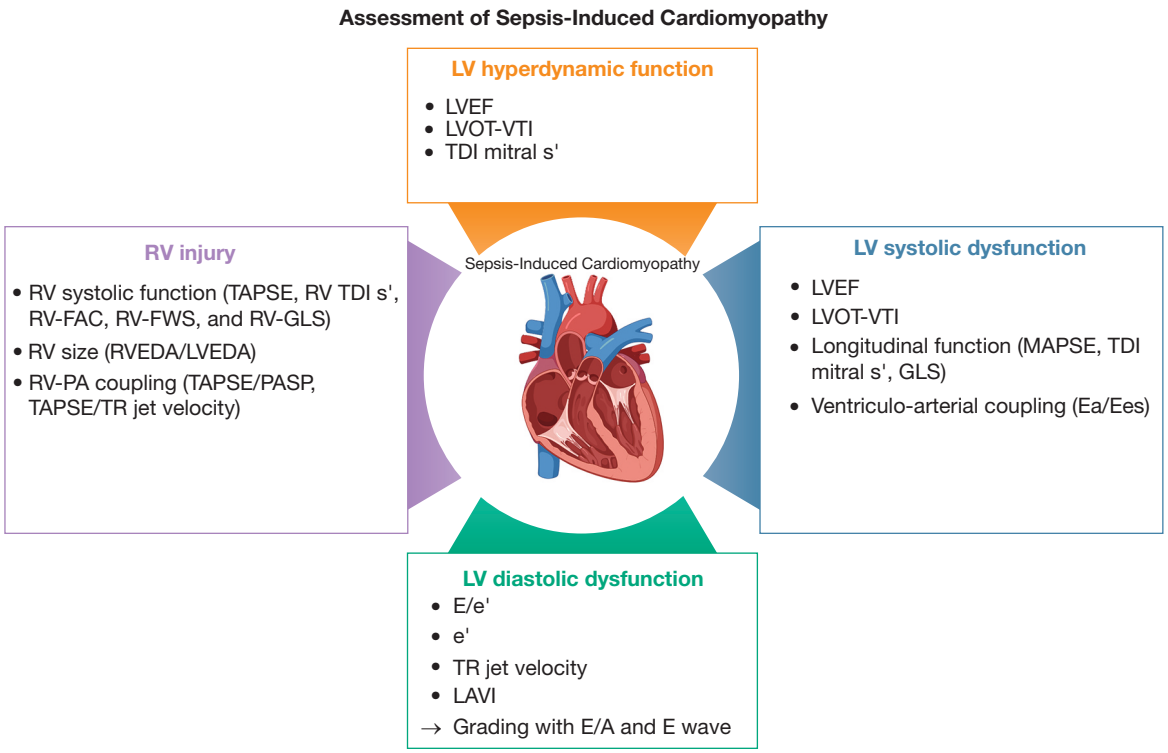

Figure 2 – *Assessment of sepsis-induced cardiomyopathy. e′ = early diastolic mitral annular velocity; E/e′ ratio = ratio of early diastolic mitral inflow velocity to early diastolic mitral annulus velocity; Ea = arterial elastance; Ees = left ventricular end-systolic elastance; FAC = fraction area change; FWS = free wall strain; GLS = global longitudinal strain; LAVI = left atrial volume index; LVEDA = left ventricular end-diastolic area; LVEF = left ventricular ejection fraction; LVOT-VTI = left ventricular outflow tract-velocity time integral; MAPSE = mitral annular plane systolic excursion; PA = pulmonary artery; PASP = pulmonary artery systolic pressure; RV = right ventricular; RVEDA = right ventricular end-diastolic area; TAPSE = tricuspid annular plane systolic excursion; TDI = tissue Doppler imaging; TDI mitral s' = tissue Doppler imaging-derived mitral s' wave velocity; TR = tricuspid regurgitation. Created with BioRender.com (Sato R; 2025; https://BioRender.com/w68g712).*

primarily reflect regional longitudinal function and are not directly interchangeable with LVEF,[25] they still provide a practical gross estimate of LV systolic function, similar to visually estimated LVEF, in which small differences rarely affect clinical decision-making.

Speckle-tracking echocardiography-derived global longitudinal strain (GLS) provides comprehensive LV longitudinal systolic function and predicts subsequent LVEF decline.[6] It remains load dependent,[26] however, and speckle-tracking echocardiography-equipped device availability in ICUs is limited. V-A coupling, representing the interaction between arterial elastance and LV end-systolic elastance, has been evaluated as a potential load-independent parameter. Although invasive pressure-volume loops are the gold standard, noninvasive methods (eg, method of Chen et al[27]) allow practical estimation in ICU settings. However, robust clinical data validating the feasibility and utility of V-A coupling in sepsis remain limited.[7]

In summary, although LVEF remains foundational, its limitations necessitate complementary parameters such as LVOT-VTI, longitudinal systolic function measures (MAPSE, TDI mitral s', and GLS), and, potentially, V-A coupling. Attention should be given to both reduced and abnormally hyperdynamic LV contractility for more comprehensive LV assessment.

LV Diastolic Function: Assessing LV diastolic dysfunction in sepsis is challenging yet crucial. The American Society of Echocardiography and the European Association of Cardiovascular Imaging guidelines recommend assessing diastolic dysfunction using the ratio of early diastolic mitral inflow velocity to early diastolic mitral annulus velocity (E/e′ ratio), early diastolic mitral annular velocity (e′), left atrial volume index, and tricuspid regurgitation jet velocity, aided by E-wave velocity and the E/A ratio to grade the diastolic dysfunction.[28] However, left atrial volume index and tricuspid regurgitation jet velocity may be limited in ICU settings as these factors may reflect chronic rather than acute changes.[29]

Thus, more pragmatic echocardiographic measures such as e' velocity and E/e' ratio have gained attention for their applicability in ICU settings. A simplified method using only septal e' velocity and the E/e' ratio exhibited diagnostic accuracy comparable to the American Society of Echocardiography 2009 guideline-based approach.[30] This method proposed diagnosing diastolic dysfunction with septal e' < 8 cm/s and grading with E/e' (grade I, ≤ 8; grade II, 8-13; grade III, ≥ 13). A subsequent study found this simplified method might correlate better with clinically meaningful outcomes related to diastolic dysfunction (need for mechanical ventilation or increased vasopressor dosages) than both 2009 and 2016 definitions.[31] However, another study in patients critically ill with novel COVID-19 reported significant discrepancies between the simplified algorithm and the 2016 guideline criteria,[32] suggesting that further validation is required.

The E/e' ratio also noninvasively estimates pulmonary arterial occlusion pressure (PAOP). Although validated formulas (eg, the formula of Nagueh et al[33]: PAOP $= 1.24 \times$ [E/e'] $+ 1.9$) exist for heart failure populations, they require further validation in patients who have sepsis and are mechanically ventilated. Importantly, PEEP can reduce e' velocities, possibly reflecting impaired LV relaxation.[34] Studies suggest that lower E/e' thresholds (approximately 7.5-9) may more reliably indicate elevated PAOP in this population compared with traditional outpatient thresholds (≥ 14).[35,36]

RV Injury: RV injury can present as RV systolic dysfunction, dilatation, or both. Visual assessment by trained intensivists reliably excludes RV pathology but tends to overestimate RV dilatation severity.[37] Tricuspid annular plane systolic excursion (TAPSE) is commonly used to define RV systolic dysfunction in critical care research.[38] However, TAPSE measures only longitudinal systolic function, overlooking radial contractility, which limits comprehensiveness.[39] Similarly, RV TDI s' velocity shares this limitation. In contrast, RV fraction area change integrates both longitudinal and radial contractility but requires optimal image quality, which is often difficult in critically ill patients.

The ratio of RV end-diastolic area to LV end-diastolic area (RVEDA/LVEDA) is another commonly used parameter to describe RV morphology. Given the compliance of the right ventricle, it can accommodate acute loading increases by dilating. RV dilatation is often defined as RVEDA/LVEDA > 0.6.[40]

Similar to function in the left ventricle, RV longitudinal systolic function has also been evaluated. A study in patients with sepsis suggested that RV free wall strain (RV-FWS) may unmask RV systolic dysfunction not detected by conventional RV assessment.[41] RV-GLS may be more comprehensive, incorporating septal and RV free wall longitudinal contraction. Values below

–20% are generally considered normal.[20] The validity of RV-FWS or RV-GLS in patients with sepsis warrants further investigation.

Recent attention has shifted from functional to hemodynamic assessment, such as RV-pulmonary artery (PA) coupling. Several methods exist, but the most practical at the bedside is the ratio of TAPSE to PA systolic pressure or tricuspid regurgitation jet velocity. Because RV-PA coupling reflects the RV adaptation to afterload, it may be an early marker of RV systolic dysfunction. However, noninvasively measured RV-PA coupling displays only moderate correlation with invasive pressure-volume loop analysis.[42]

Given the ability of the right ventricle to adapt to acute loading changes, without significant pressure increases, RV dilatation typically precedes measurable RV systolic dysfunction. Therefore, RV injury in sepsis should be conceptualized as a continuum, from dilatation (RVEDA/LVEDA $>$ 0.6), through progressive RV-PA decoupling, to overt systolic function (detectable via TAPSE, RV TDI s', RV fraction area change, and RV-FWS/GLS).

Cardiac MRI: Cardiac MRI has the unique capability to evaluate not only myocardial function but also myocardial edema, inflammation, and fibrosis. In a prospective study evaluating SICM by using cardiac MRI, patients with sepsis with reduced LVEF exhibited global myocardial edema and inflammation.[43] Importantly, this study also assessed RV volumes and RV ejection fraction, and all patients with reduced LVEF concurrently exhibited reduced RV ejection fraction. Unlike echocardiography, cardiac MRI is often limited by patients' clinical instability, and it is not easy to perform in the ICU setting.

Biomarkers: B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP), reflecting cardiac wall stress, correlate more with the severity of critical illness than with SICM.[44] Both BNP and NT-proBNP increase significantly more in septic shock than in cardiogenic shock.[45] NT-proBNP, using a threshold of 3,165 pg/L, has been shown to differentiate septic shock from other shock types, including cardiogenic shock, with 96.0% sensitivity and 88.0% specificity.[46]

Troponin is another routinely used biomarker for myocardial injury. A meta-analysis indicated that troponin elevation in sepsis is associated with LV dilatation and systolic dysfunction.[47] In addition, elevated high-sensitivity troponin has been reported to predict both LV systolic and diastolic dysfunction in sepsis.[48] Nevertheless, both BNP and troponin elevations lack specificity in the context of sepsis, making their use for SICM assessment challenging.

Prognosis

New-onset LV systolic dysfunction (within 72 hours of sepsis) has been associated with significantly increased mortality.[14] Both V-A decoupling and higher (worse) GLS values have also been associated with higher mortality in patients with sepsis.[49,50] In line with these findings, a U-shaped relationship between LVEF and in-hospital mortality was observed, with both severe LV dysfunction (LVEF $<$ 25%) and hyperdynamic LV function (LVEF $>$ 70%) associated with significantly higher mortality.[51] Although SICM is believed to recover quickly in survivors,[1] cardiac MRI has revealed diffuse LV myocardial fibrosis without myocardial edema, resembling nonischemic cardiomyopathies.[52] Given that sepsis survivors are at increased risk of late cardiovascular events,[53] evaluation of SICM's long-term impact is warranted.

A meta-analysis showed that lower e' velocities, higher E/e' ratios, and other diastolic dysfunction parameters were strongly associated with higher mortality in patients with sepsis.[54] Another meta-analysis found that elevated E/e', lower e' velocities, and higher E velocity were significantly associated with a greater risk of failure to wean the patient from mechanical ventilation, whereas LVEF alone was not predictive.[55] However, a large multicenter French study found no association with mortality,[16] warranting further evaluation.

RV injury, including both RV systolic dysfunction and dilatation, was associated with significantly higher short- and long-term mortality.[18] RV-PA coupling has also been associated with increased mortality.[56] One study proposed a composite RV injury score incorporating 3 echocardiographic parameters: RV systolic dysfunction, RV dilation, and RV-PA decoupling.[57] Each parameter was independently associated with increased 30-day mortality, with adjusted hazard ratios of 2.25 for RV systolic dysfunction, 2.19 for RV dilatation, and 2.08 for RV-PA coupling. The presence of multiple abnormalities had an additive effect on prognosis. The adjusted hazard ratios for 30-day mortality increased stepwise to 2.94 with 1 abnormality, 3.20 with 2, and 7.17 when all 3 were present. These findings suggest the cumulative prognostic impact of RV injury components in patients with sepsis.

Many studies have lacked comprehensive assessment of myocardial dysfunction. A more holistic approach was taken by Geri et al[58] that identified 5 distinct cardiovascular profiles via cluster analysis: (1) well-resuscitated without LV or RV dysfunction; (2) LV systolic dysfunction; (3) hyperkinetic profile; (4) RV failure; and (5) persistent hypovolemia. Each profile was associated with different mortality risks, with LV systolic dysfunction being highest (50.0%), followed by RV failure (42.0%), persistent hypovolemia (38.6%), hyperkinetic profile (23.8%), and well-resuscitated group (21.3%). Although patients were grouped into mutually exclusive phenotypes, substantial overlap in cardiac parameters suggests that myocardial dysfunction in sepsis exists on a continuum.

These findings reinforce SICM as a complex syndrome of overlapping, dynamic phenotypes, not a uniform entity. This necessitates a paradigm shift; that is, recognizing SICM as a spectrum of myocardial injury rather than as a binary diagnosis. Precisely characterizing cardiovascular phenotypes provides the framework for phenotype-guided management.

Management

Effective management of SICM requires acknowledging its spectrum of myocardial phenotypes, each with unique prognostic and therapeutic implications (Fig 3). Understanding these phenotypes allows for tailored interventions beyond 1-size-fits-all resuscitation strategies.

LV Systolic Dysfunction: Managing LV systolic dysfunction in sepsis is complex, requiring careful balance between restoring afterload and maintaining cardiac output. Although vasopressin is frequently used as a second-line vasopressor in septic shock, and recent studies suggest benefits with its early initiation in patients with sepsis,[59,60] its impact when initiated early in patients with LV systolic dysfunction remains unclear. Current data are limited to a retrospective study including 27 patients with LV systolic dysfunction (LVEF $<$ 45%), indicating that these patients responded poorly to vasopressin.[61] In contrast, in a small retrospective study of cardiogenic shock, vasopressin improved BP in approximately one-half of patients, and preserved cardiac reserve enabling adaptation to an increased arterial load

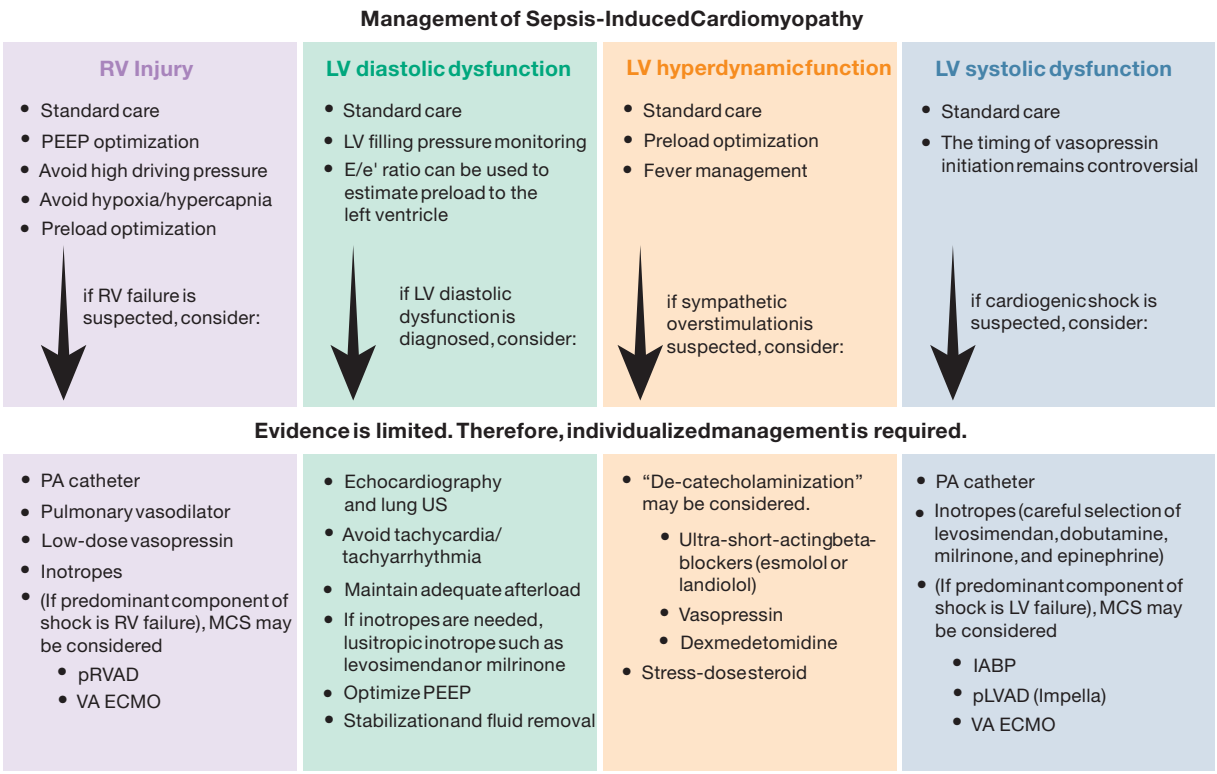

Figure 3 – *Management of sepsis-induced cardiomyopathy. IABP = intra-aortic balloon pump; MCS = mechanical circulatory support; LV = left ventricular; PA = pulmonary artery; PEEP = positive end expiratory pressure; pLVAD = peripheral left ventricular assist device; pRVAD = peripheral right ventricular assist device; RV = right ventricular; US = ultrasound; VA ECMO = venoarterial extracorporeal membrane oxygenation. Created with BioRender.com (Sato R; 2025; https://BioRender.com/q69v319).*

induced by vasopressin was suggested as the key determinant of responsiveness.[62]

Given the retrospective nature and small sample size of these studies, whether norepinephrine titration should be prioritized over early vasopressin initiation in this specific population requires further evaluation. The Surviving Sepsis Campaign (SSC) guidelines propose adding dobutamine to norepinephrine or using epinephrine if myocardial dysfunction contributes to hypoperfusion despite adequate fluid resuscitation and BP,[63] suggesting a cardiac component to shock. However, supporting evidence remains inconclusive. A retrospective study found that inotropes, including dobutamine and epinephrine, were associated with significantly higher mortality in septic shock.[64] A prospective study showed that although dobutamine improved echocardiographic parameters, it often worsened vasoplegia in patients with sepsis with myocardial dysfunction.[65]

Levosimendan may improve cardiac function without increasing myocardial oxygen demand. However, a large randomized controlled trial (Levosimendan for the Prevention of Acute Organ Dysfunction in Sepsis [LeoPARDS]) failed to show a reduction in organ failure or mortality in patients with sepsis treated with levosimendan.[66] Notably, this study was not phenotype-guided and included a heterogenous population with high median cardiac index with no echocardiographic assessment prior to inclusion. In contrast, a smaller randomized trial reported improved myocardial function with levosimendan in patients with severe SICM.[67] In addition, a prospective observational study found that levosimendan was associated with improved survival in patients with severe SICM.[68] A meta-analysis further supports its hemodynamic benefits, showing superiority over dobutamine in improving the cardiac index and LV stroke work index in patients with sepsis with myocardial dysfunction.[69] Milrinone also provides inotropic support but has notable vasodilatory effects, warranting caution in sepsis treatment. Milrinone showed no mortality benefit over dobutamine in treatment of cardiogenic shock.[70] Given the limited and weak evidence favoring any specific inotrope, selection must be individualized, balancing potential benefits and risks, with close hemodynamic monitoring. PA catheterization may aid continuous hemodynamic monitoring and guide therapy, potentially improving outcomes when cardiogenic shock is present.[71]

Mechanical circulatory support (MCS), such as intraaortic balloon pump, percutaneous LV assist device,[72] and venoarterial extracorporeal membrane oxygenation,[73] may be considered in selected severe cases; their role remains controversial, however. MCS should be reserved for cases in which SICM clearly drives shock, as outcomes may worsen if applied while vasoplegia persists.[74]

LV Hyperdynamic Systolic Function: Hyperdynamic LV function requires correction of reversible causes such as fever, increased metabolic demand, inadequate fluid resuscitation, or vasoplegia. If it persists despite addressing these factors, it may represent a "noncompensatory" state, often accompanied by persistent tachycardia. In such cases, "de-catecholaminization" strategies might be considered, but it is important to confirm that hypovolemia and vasoplegia are not the predominant unaddressed issues, as these strategies can be detrimental.

A pilot randomized controlled trial revealed that treating persistent tachycardia with esmolol, an ultra-short-acting, highly selective beta$_1$-blocker, reduced mortality in patients with septic shock.[75] Although an earlier meta-analysis indicated improved 28-day survival with esmolol or landiolol,[76] an updated meta-analysis including 3 recent multicenter randomized controlled trials suggested the fragility of this evidence and emphasized the need for further investigation.[77] In these studies, ultra-short-acting beta-blockers increased stroke volume index and reduced heart rate without negatively affecting cardiac index or BP, suggesting potential improvement in cardiovascular efficiency.

Vasopressin, a non-catecholaminergic vasoconstrictor, can be considered as a potential strategy to reduce catecholamine exposure. However, its impact on cardiac function in SICM remains controversial. Although early vasopressin initiation seems theoretically reasonable, especially in patients with hyperdynamic LV function, a retrospective study showed no significant differences in response among patients with hyperdynamic LV function.[61] In addition, some evidence suggests a potential positive inotropic effect at a low dose.[78] Given the limited clinical evidence, routine early initiation of vasopressin specifically for de-catecholaminization in patients with SICM warrants further data, and a highly individualized approach is required.

Dexmedetomidine has also been investigated in sepsis. Although it may modulate sympathetic tone and reduce norepinephrine dosage,[79] mortality results have been inconsistent.[80,81] The most recent trial was terminated due to higher mortality and reduced norepinephrine response with dexmedetomidine in patients with sepsis receiving high-dose vasopressors.[81] Thus, caution is warranted in hyperdynamic sepsis, especially with high vasopressor needs. De-catecholaminization requires highly individualized management.

Stress doses of hydrocortisone might also attenuate the hyperdynamic state in septic shock,[82] possibly by mitigating excessive inflammation and improving vascular tone. This theory requires further investigation in this population.

LV Diastolic Dysfunction: Although there is no specific recommendation in the SSC guidelines, an approach labeled the "CHEOPS" bundle has been proposed as expert opinion for managing LV diastolic dysfunction in critically ill patients.[83] This algorithm includes "chest ultrasound" (echocardiography and lung ultrasound) for diagnosis; managing "hemodynamics" (treating tachycardia/tachyarrhythmia to ensure enough diastolic time, maintaining adequate afterload, consideration for inotropes with lusitropic effects such as levosimendan[84] or milrinone[85] if inotropes are needed); "optimizing PEEP" (to facilitate LV ejection and optimize pulmonary vascular resistance); and "stabilization and fluid removal" (diuresis or renal replacement therapy once hemodynamically feasible). Although levosimendan may offer the most consistent lusitropic effect among inotropes, its supporting evidence comes primarily from studies in heart failure or cardiac surgery rather than sepsis. Further studies are needed to validate this approach in patients with sepsis. Meanwhile, in a prospective multicenter French study that showed no association between LV diastolic dysfunction and mortality, patients with more advanced diastolic dysfunction were not blinded to intensivists and received significantly lower fluid volumes, suggesting that timely recognition and tailored fluid management may attenuate its prognostic impact.[16]

RV Injury: Effective management requires understanding the mechanisms influencing RV function, including fluid balance, pharmacology, and mechanical ventilation.

Excessive fluid resuscitation increases the risks of RV dilation and dysfunction, whereas overly restrictive strategies can impair cardiac output. Thus, fluid management guided by clinical and hemodynamic assessment is essential. Inotropes are often used for RV injury. Both dobutamine and milrinone improve RV systolic function,[86,87] although their clinical impact on outcomes remains unknown. Vasopressin acts primarily as a systemic vasoconstrictor via V1 receptors, and animal studies suggest it may exert indirect pulmonary vasodilatory effects, potentially by attenuating catecholamine-mediated vasoconstriction via stimulation of nitric oxide production or redistribution of blood flow by selectively sparing pulmonary vasculature.[88] However, clinical evidence is limited; a retrospective study showed no difference in vasopressin response among patients with septic shock and RV injury,[61] suggesting the need for further investigation.

Given the impact of mechanical ventilation on RV, PEEP should be optimized to balance oxygenation and RV afterload. Driving pressure ≥ 18 cm H_2O, $Pa_{CO_2} \geq 48$ cm$_2$O, and a Pa_{O_2}/F_{IO_2} ratio < 150 mm Hg are risk factors for RV injury in ARDS.[89] RV-protective ventilation with limited driving pressure, avoidance of hypercapnia and hypoxia, and optimal PEEP should be used.

If RV injury continues to cause low cardiac output despite optimized medical management, MCS such as percutaneous RV assist devices (eg, Impella RP [Abiomed] or Protek Duo [LivaNova]) may be considered. Evidence on the feasibility and outcomes of RV-specific MCS in sepsis is lacking, and decisions should be highly individualized based on clinical expertise, patient-specific hemodynamics, and institutional capabilities.

Future Directions

Due to lack of baseline assessments of myocardial function, many studies are unable to identify new-onset myocardial dysfunction. Consequently, these studies cannot distinguish between preexisting myocardial abnormalities and dysfunction arising directly from sepsis. Therefore, prospective longitudinal studies that establish baseline myocardial function and track its trajectory across each SICM phenotype during the course of sepsis are needed. These studies should ideally include serial, standardized cardiac evaluations to better elucidate the natural progression and recovery patterns of myocardial dysfunction.

Although many echocardiographic parameters have been proposed to define SICM, there remains no

universally accepted definition. In addition, many studies have performed limited assessments, failing to encompass the full spectrum of myocardial dysfunction. Thus, achieving expert consensus on defining SICM that considers its different phenotypes is warranted.

Lastly, therapeutic approaches tailored specifically to SICM phenotypes should be investigated through prospective clinical trials. Although the SSC guidelines recommend generalized hemodynamic management strategies, individual cardiac phenotypes may require phenotype-specific management approaches to optimize outcomes.

Summary

SICM is a common organ dysfunction in sepsis and septic shock. It is a highly heterogeneous entity arising from multiple mechanisms, including biochemical mediators, mitochondrial dysfunction, myocardial ischemia, and dynamic loading conditions. Clinical features may include LV systolic dysfunction or LV hyperdynamic systolic function, and/or LV diastolic dysfunction and/or RV injury, which can occur independently or in combination. These phenotypes are relatively common and associated with higher mortality. Although no specific therapeutic strategy has been proven to improve outcomes, SICM requires phenotype-guided, individualized approaches.

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